Statement

Evaluation and Management of Hypertension

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Systemic hypertension is an important condition in childhood, with estimated population prevalence of 1-2% in the developed countries(1). Nutritional surveys, in the USA show a significant secular increase in systolic and diastolic blood pressures(1). The causes for increase in blood pressure are attributed to obesity, change in dietary habits, decreased physical activity and increasing stress. Similar data is lacking from India; small surveys in school children suggest a prevalence ranging from 2-5%(2).

Hypertension is classified as essential (primary) or secondary to, *e.g.,* a renal parenchymal, renovascular or an endocrine disorder. Most children with sustained, severe or symptomatic hypertension have an underlying etiology, and are at risk for acute and chronic complications. Screening studies suggest that essential hypertension is also important during late childhood and adolescence. There is increasing evidence that essential hypertension tracks into adulthood, resulting in considerable cardio-vascular morbidity(3).

In view of concerns regarding hypertension in childhood and its long-term consequences, a Consensus Meeting of Experts of the Indian Pediatric Nephrology Group was held in Bangalore on 25 November 2005 in order to:

1. Recommend criteria for screening and defining hypertension in children;
2. Outline the evaluation of children detected to have hypertension; and
3. Suggest an approach to treatment.

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Definitions and Staging of Hypertension

Tables I and II show normative data on blood pressure values, based on age and height percentiles, derived from a large multiethnic cohort of children in USA(4). The Expert Group endorses the guidelines on definition of hypertension proposed in the Fourth US Task Force Report on Hypertension(4), which are in broad conformity with the Seventh Joint National Commission Report for adults(5). Assessment of both systolic and diastolic pressures is important and interpreted in relation to age and height related normative data. If percentiles of systolic and diastolic pressures are different, the higher percentile is used for defining and staging hypertension. Normative data from the Second Report should be used for defining hypertension in infancy(6).

- Pre-hypertension is defined as systolic or diastolic blood pressure between the 90th and 95th percentile. Adolescents having blood pressure >120/80 mm Hg, but below the 95th percentile are also included in this category.
- Hypertension is defined as systolic or diastolic blood pressure exceeding the 95th percentile for age, gender and height, on at least three separate occasions, 1-3 weeks apart.

Since the severity of hypertension influences its management, it should be staged as below.

- *Stage 1 hypertension:* Systolic or diastolic blood pressure values exceeding the 95th

TABLE I–*Blood Pressure (BP) Levels for Boys by Age and Height Percentile*

Age (yr)	BP percentile	Systolic BP (mm Hg)							Diastolic BP (mm Hg)						
		Height percentile							Height percentile						
		5th	10th	25th	50th	75th	90th	95th	5th	10th	25th	50th	75th	90th	95th
1	50th	80	81	83	85	87	88	89	34	35	36	37	38	39	39
	90th	94	95	97	99	100	102	103	49	50	51	52	53	53	54
	95th	98	99	101	103	104	106	106	54	54	55	56	57	58	58
	99th	105	106	108	110	112	113	114	61	62	63	64	65	66	66
2	50th	84	85	87	88	90	92	92	39	40	41	42	43	44	44
	90th	97	99	100	102	104	105	106	54	55	56	57	58	58	59
	95th	101	102	104	106	108	109	110	59	59	60	61	62	63	63
	99th	109	110	111	113	115	117	117	66	67	68	69	70	71	71
3	50th	86	87	89	91	93	94	95	44	44	45	46	47	48	48
	90th	100	101	103	105	107	108	109	59	59	60	61	62	63	63
	95th	104	105	107	109	110	112	113	63	63	64	65	66	67	67
	99th	111	112	114	116	118	119	120	71	71	72	73	74	75	75
4	50th	88	89	91	93	95	96	97	47	48	49	50	51	51	52
	90th	102	103	105	107	109	110	111	62	63	64	65	66	66	67
	95th	106	107	109	111	112	114	115	66	67	68	69	70	71	71
	99th	113	114	116	118	120	121	122	74	75	76	77	78	78	79
5	50th	90	91	93	95	96	98	98	50	51	52	53	54	55	55
	90th	104	105	106	108	110	111	112	65	66	67	68	69	69	70
	95th	108	109	110	112	114	115	116	69	70	71	72	73	74	74
	99th	115	116	118	120	121	123	123	77	78	79	80	81	81	82
6	50th	91	92	94	96	98	99	100	53	53	54	55	56	57	57
	90th	105	106	108	110	111	113	113	68	68	69	70	71	72	72
	95th	109	110	112	114	115	117	117	72	72	73	74	75	76	76
	99th	116	117	119	121	123	124	125	80	80	81	82	83	84	84
7.	50th	92	94	95	97	99	100	101	55	55	56	57	58	59	59
	90th	106	107	109	111	113	114	115	70	70	71	72	73	74	74
	95th	110	111	113	115	117	118	119	74	74	75	76	77	78	78
	99th	117	118	120	122	124	125	126	82	82	83	84	85	86	86
8	50th	94	95	97	99	100	102	102	56	57	58	59	60	60	61
	90th	107	109	110	112	114	115	116	71	72	72	73	74	75	76
	95th	111	112	114	116	118	119	120	75	76	77	78	79	79	80
	99th	119	120	122	123	125	127	127	83	84	85	86	87	87	88
9	50th	95	96	98	100	102	103	104	57	58	59	60	61	61	62
	90th	109	110	112	114	115	117	118	72	73	74	75	76	76	77
	95th	113	114	116	118	119	121	121	76	77	78	79	80	81	81
	99th	120	121	123	125	127	128	129	84	85	86	87	88	88	89

TABLE I *(Contd.)*–*Blood Pressure (BP) Levels for Boys by Age and Height Percentile*

Age (yr)	BP percentile	Systolic BP (mm Hg)							Diastolic BP (mm Hg)						
		Height percentile							Height percentile						
		5th	10th	25th	50th	75th	90th	95th	5th	10th	25th	50th	75th	90th	95th
10	50th	97	98	100	102	103	105	106	58	59	60	61	61	62	63
	90th	111	112	114	115	117	109	119	73	73	74	75	76	77	78
	95th	115	116	117	119	121	122	123	77	78	79	80	81	81	82
	99th	122	123	125	127	128	130	130	85	86	86	88	88	89	90
11	50th	99	100	102	104	105	107	107	59	59	60	61	62	63	63
	90th	113	114	115	117	119	120	121	74	74	75	76	77	78	78
	95th	117	118	119	121	123	124	125	78	78	79	80	81	82	82
	99th	124	125	127	129	130	132	132	86	86	87	88	89	90	90
12	50th	101	102	104	106	108	109	110	59	60	61	62	63	63	64
	90th	115	116	118	120	121	123	123	74	75	75	76	77	78	79
	95th	119	120	122	123	125	127	127	78	79	80	81	82	82	83
	99th	126	127	129	131	133	134	135	86	87	88	89	90	90	91
13	50th	104	105	106	108	110	111	112	60	60	61	62	63	64	64
	90th	117	118	120	122	124	125	126	75	75	76	77	78	79	79
	95th	121	122	124	126	128	129	130	79	79	80	81	82	83	83
	99th	128	130	131	133	135	136	137	87	87	88	89	90	91	91
14	50th	106	107	109	111	113	114	115	60	61	62	63	64	65	65
	90th	120	121	123	125	126	128	128	75	76	77	78	79	79	80
	95th	124	125	127	128	130	132	132	80	80	81	82	83	84	84
	99th	131	132	134	136	138	139	140	87	87	89	90	91	92	92
15	50th	109	110	112	113	115	117	117	61	62	63	64	65	66	66
	90th	122	124	125	127	129	130	131	76	77	78	79	80	80	81
	95th	126	127	129	131	133	134	135	81	81	82	83	84	85	85
	99th	134	135	136	138	140	142	142	88	89	90	91	92	93	93
16	50th	111	112	114	116	118	119	120	63	63	64	65	66	67	67
	90th	125	126	128	130	131	133	134	78	78	79	80	81	82	82
	95th	129	130	132	134	135	137	137	82	83	83	84	85	86	87
	99th	136	137	139	141	143	144	145	90	90	91	92	93	94	94
17	50th	114	115	116	118	120	121	122	65	66	66	67	68	69	70
	90th	127	128	130	132	134	135	136	80	80	81	82	83	84	84
	95th	131	132	134	136	138	139	140	84	85	86	87	87	88	89
	99th	139	140	141	143	145	146	147	92	93	93	94	95	96	97

TABLE II–*Blood Pressure (BP) Levels for Girls by Age and Height Percentile*

Age (yr)	BP percentile	Systolic BP (mm Hg)							Diastolic BP (mm Hg)						
		Height percentile							Height percentile						
		5th	10th	25th	50th	75th	90th	95th	5th	10th	25th	50th	75th	90th	95th
1	50th	83	84	85	86	88	89	90	38	39	39	40	41	41	42
	90th	97	97	98	100	101	102	103	52	53	53	54	55	55	56
	95th	100	101	102	104	105	106	107	56	57	57	58	59	59	60
	99th	108	108	109	111	112	113	114	64	64	65	65	66	67	67
2	50th	85	85	87	88	89	91	91	43	44	44	45	46	46	47
	90th	98	99	100	101	103	104	105	57	58	58	59	60	61	61
	95th	102	103	104	105	107	108	109	61	62	62	63	64	65	65
	99th	109	110	111	112	114	115	116	69	69	70	70	71	72	72
3	50th	86	87	88	89	91	92	93	47	48	48	49	50	50	51
	90th	100	100	102	103	104	106	106	61	62	62	63	64	64	65
	95th	104	104	105	107	108	109	110	65	66	66	67	68	68	69
	99th	111	111	113	114	115	116	117	73	73	74	74	75	76	76
4	50th	88	88	90	91	92	94	94	50	50	51	52	52	53	54
	90th	101	102	103	104	106	107	108	64	64	65	66	67	67	68
	95th	105	106	107	108	110	111	112	68	68	69	70	71	71	72
	99th	112	113	114	115	117	118	119	76	76	76	77	78	79	79
5	50th	89	90	91	93	94	95	96	52	53	53	54	55	55	56
	90th	103	103	105	106	107	109	109	66	67	67	68	69	69	70
	95th	107	107	108	110	111	112	113	70	71	71	72	73	73	74
	99th	114	114	116	117	118	120	120	78	78	79	79	80	81	81
6	50th	91	92	93	94	96	97	98	54	54	55	56	56	57	58
	90th	104	105	106	108	109	110	111	68	68	69	70	70	71	72
	95th	108	109	110	111	113	114	115	72	72	73	74	74	75	76
	99th	115	116	117	119	120	121	122	80	80	80	81	82	83	83
7.	50th	93	93	95	96	97	99	99	55	56	56	57	58	58	59
	90th	106	107	108	109	111	112	113	69	70	70	71	72	72	73
	95th	110	111	112	113	115	116	116	73	74	74	75	76	76	77
	99th	117	118	119	120	122	123	124	81	81	82	82	83	84	84
8	50th	95	95	96	98	99	100	101	57	57	57	58	59	60	60
	90th	108	109	110	111	113	114	114	71	71	71	72	73	74	74
	95th	112	112	114	115	116	118	118	75	75	75	76	77	78	78
	99th	119	120	121	122	123	125	125	82	82	83	83	84	85	86
9	50th	96	97	98	100	101	102	103	58	58	58	59	60	61	61
	90th	110	110	112	113	114	116	116	72	72	72	73	74	75	75
	95th	114	114	115	117	118	119	120	76	76	76	77	78	79	79
	99th	121	121	123	124	125	127	127	83	83	84	84	85	86	87

TABLE II *(Contd.)* – *Blood Pressure (BP) Levels for Girls by Age and Height Percentile*

Age (yr)	BP percentile	Systolic BP (mm Hg)							Diastolic BP (mm Hg)						
		Height percentile							Height percentile						
		5th	10th	25th	50th	75th	90th	95th	5th	10th	25th	50th	75th	90th	95th
10	50th	98	99	100	102	103	104	105	59	59	59	60	61	62	62
	90th	112	112	114	115	116	118	118	73	73	73	74	75	76	76
	95th	116	116	117	119	120	121	122	77	77	77	78	79	80	80
	99th	123	123	125	126	127	129	129	84	84	85	86	86	87	88
11	50th	100	101	102	103	105	106	107	60	60	60	61	62	63	63
	90th	114	114	116	117	118	119	120	74	74	74	75	76	77	77
	95th	118	118	119	121	122	123	124	78	78	78	79	80	81	81
	99th	125	125	126	128	129	130	131	85	85	86	87	87	88	89
12	50th	102	103	104	105	107	108	109	61	61	61	62	63	64	64
	90th	116	116	117	119	120	121	122	75	75	75	76	77	78	78
	95th	119	120	121	123	124	125	126	79	79	79	80	81	82	82
	99th	127	127	128	130	131	132	133	86	86	87	88	88	89	90
13	50th	104	105	106	107	109	110	110	62	62	62	63	64	65	65
	90th	117	118	119	121	122	123	124	76	76	76	77	78	79	79
	95th	121	122	123	124	126	127	128	80	80	80	81	82	83	83
	99th	128	129	130	132	133	134	135	87	87	88	89	89	90	91
14	50th	106	106	107	109	110	111	112	63	63	63	64	65	66	66
	90th	119	120	121	122	124	125	125	77	77	77	78	79	80	80
	95th	123	123	125	126	127	129	129	81	81	81	82	83	84	84
	99th	130	131	132	133	135	139	136	88	88	89	90	90	91	92
15	50th	107	108	109	110	111	113	113	64	64	64	65	66	67	67
	90th	120	121	122	123	125	126	127	78	78	78	79	80	81	81
	95th	124	125	126	127	129	130	131	82	82	82	83	84	85	85
	99th	131	132	133	134	136	137	138	89	89	90	91	91	92	93
16	50th	108	108	110	111	112	114	114	64	64	65	66	66	67	68
	90th	121	122	123	124	126	127	128	78	78	79	80	81	81	82
	95th	125	126	127	128	130	131	132	82	82	83	84	85	85	86
	99th	132	133	134	135	137	138	139	90	90	90	91	92	93	93
17	50th	108	109	110	111	113	114	115	64	65	65	66	67	67	68
	90th	122	122	123	125	126	127	128	78	79	79	80	81	81	82
	95th	125	126	127	129	130	131	132	82	83	83	84	85	85	86
	99th	133	133	134	136	137	138	139	90	90	91	91	92	93	93

percentile and up to 5 mm above the 99th percentile. Blood pressures in this range should be rechecked at least twice in the next 1-3 weeks, or sooner if symptomatic, before the patient is diagnosed to have sustained hypertension.

- *Stage 2 hypertension:* Systolic or diastolic blood pressure values 5 mm or more above the 99th percentile. The presence of stage 2 hypertension should be confirmed on a repeat measurement, at the same visit. These patients require further evaluation within one week or immediately if they are symptomatic.

Figures 1 and 2 provide charts for screening and staging of hypertension in boys and girls respectively. These have been prepared, by the Expert Group, using data from *Tables I and II* at the 50th percentile for the height for age. For example, in a 5-year-old girl with height at the 50th percentile, systolic blood pressure between 110 and 122 mm Hg and diastolic pressure between 72 and 84 mm Hg represent stage 1 hypertension. Blood pressure values exceeding 122/84 mm Hg represent stage 2 hypertension (*Fig. 2*). Blood pressure values are typically 3-5 mm lower or higher in subjects with height at the 10th or 95th percentile respectively.

While the screening charts are useful for rapid evaluation, detailed tables in Tables I-II should be consulted before initiating therapy.

White coat hypertension

Some children may show blood pressure higher than the 95th percentile in clinic or hospital setting, while it is below 90th percentile in familiar environments(7). These patients do not need pharmacological treatment, but require blood pressure monitoring over the next 12 months, since a proportion is at risk of sustained essential hypertension.

Screening for hypertension

The awareness that essential hypertension has its origin in childhood has resulted in increased emphasis on screening. The Group recommends annual measurement of blood pressure in all children more than 3-year-old, who are seen in clinics or hospital settings. Blood pressure should also be measured in at-risk younger children with: (*i*) history of prematurity, very low birth weight or interventions in NICU; (*ii*) congenital heart disease; (*iii*) recurrent urinary tract infections, known renal or urological diseases, hematuria or proteinuria; (*iv*) family history of congenital renal disorders; (*v*) malignancy, post organ transplant; (*vi*) conditions associated with hypertension, *e.g*., neurofibromatosis, tuberous sclerosis and ambiguous genitalia. Blood pressure should be measured in patients who present with features of kidney or heart disease, seizures, altered sensorium and headache or visual complaints.

Accurate techniques for measurement of blood pressure are necessary for its diagnosis, staging and follow up(8).

Measurement devices

Mercury sphygmomanometer: Normative values for blood pressure are based on sphygmomanometry, which continues to be the preferred method for blood pressure estimation. While it is recommended that blood pressure devices be calibrated and validated regularly, this process is cumbersome(9). Physicians should be aware that mercury is a major environmental pollutant and that accidental mercury spills must be managed appropriately. (For guidelines, refer to US Environment Protection Agency; www.epa.gov).

Oscillometric devices: These devices are increasingly used in infants (in whom auscultation is difficult) and in intensive care settings when frequent blood pressure measurements are needed. However, neither are most oscillometric devices validated for children, nor are there normative data based on these readings(10). Blood pressure values on oscillometry, which exceed the 90th percentile must therefore be confirmed by sphygmomanometry.

Aneroid and other devices: These instruments, based on spring-based technology require frequent calibration and validation. The use of aneroid devices and wrist or finger band oscillometry for blood pressure measurements is discouraged.

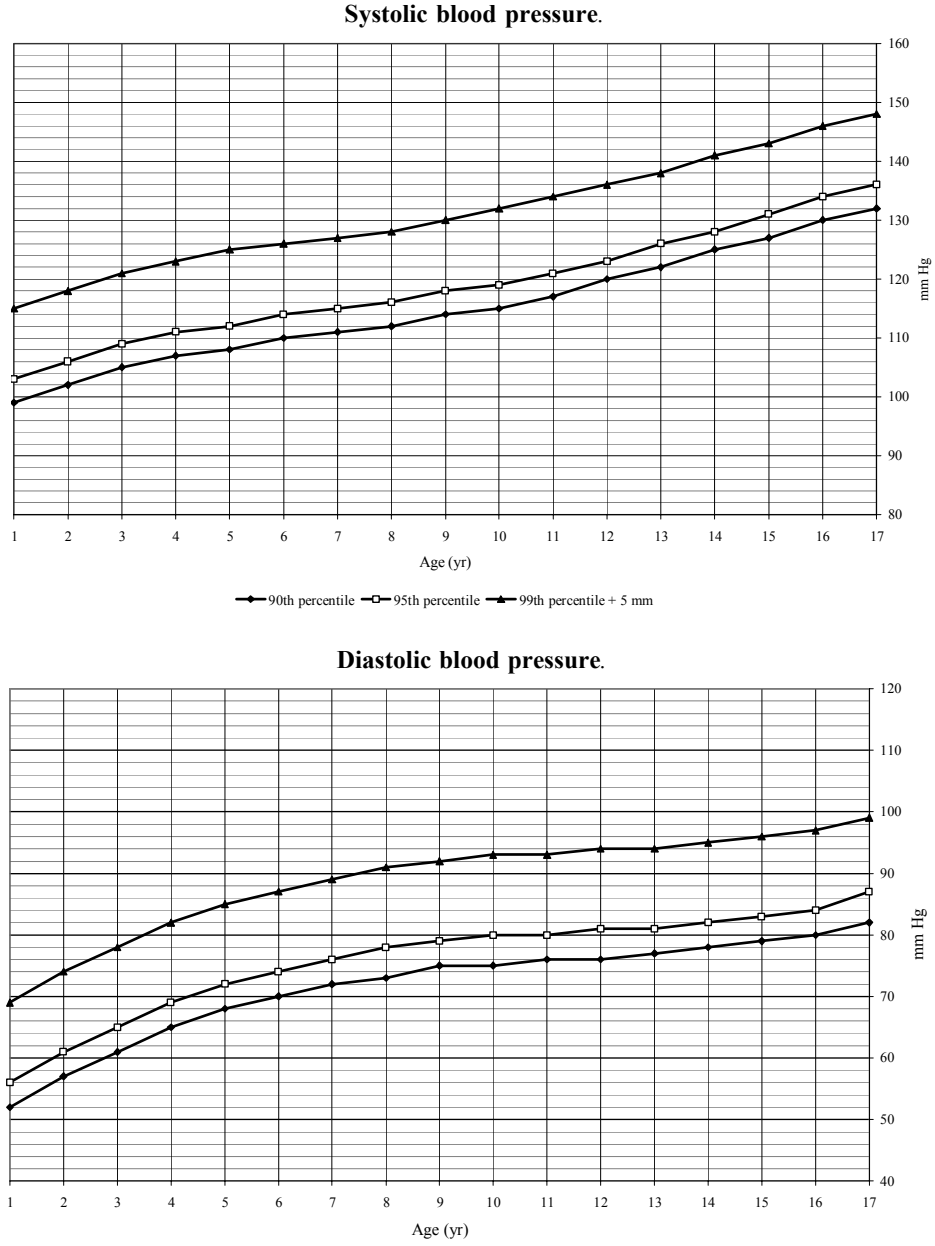

Fig. 1. *Blood pressure levels for boys at 50th percentile for height. Chart depicting 90th (closed diamonds), 95th (open circles) and 99th + 5 mm (closed triangles) percentile values for (a) systolic and (b) diastolic blood pressures, representing cut off values for the diagnosis of pre-hypertension, stage I and stage II hypertension respectively in boys (based on reference 4).*

Ambulatory blood pressure monitoring (ABPM): Continuous recordings over 12- or 24-hr are believed to reflect true blood pressures accurately, are more reproducible and correlate with target organ damage. A lack of availability of these instruments and normative standards has limited the utility of ABPM for the diagnosis of hypertension in children(4).

Sphygmomanometry

Blood pressure is recorded once the child has rested for 5-10 minutes. The measurement is done either in sitting or supine position, the latter preferred for younger children. The right arm is used for consistency and for comparison with standard tables; the cubital fossa should be at heart

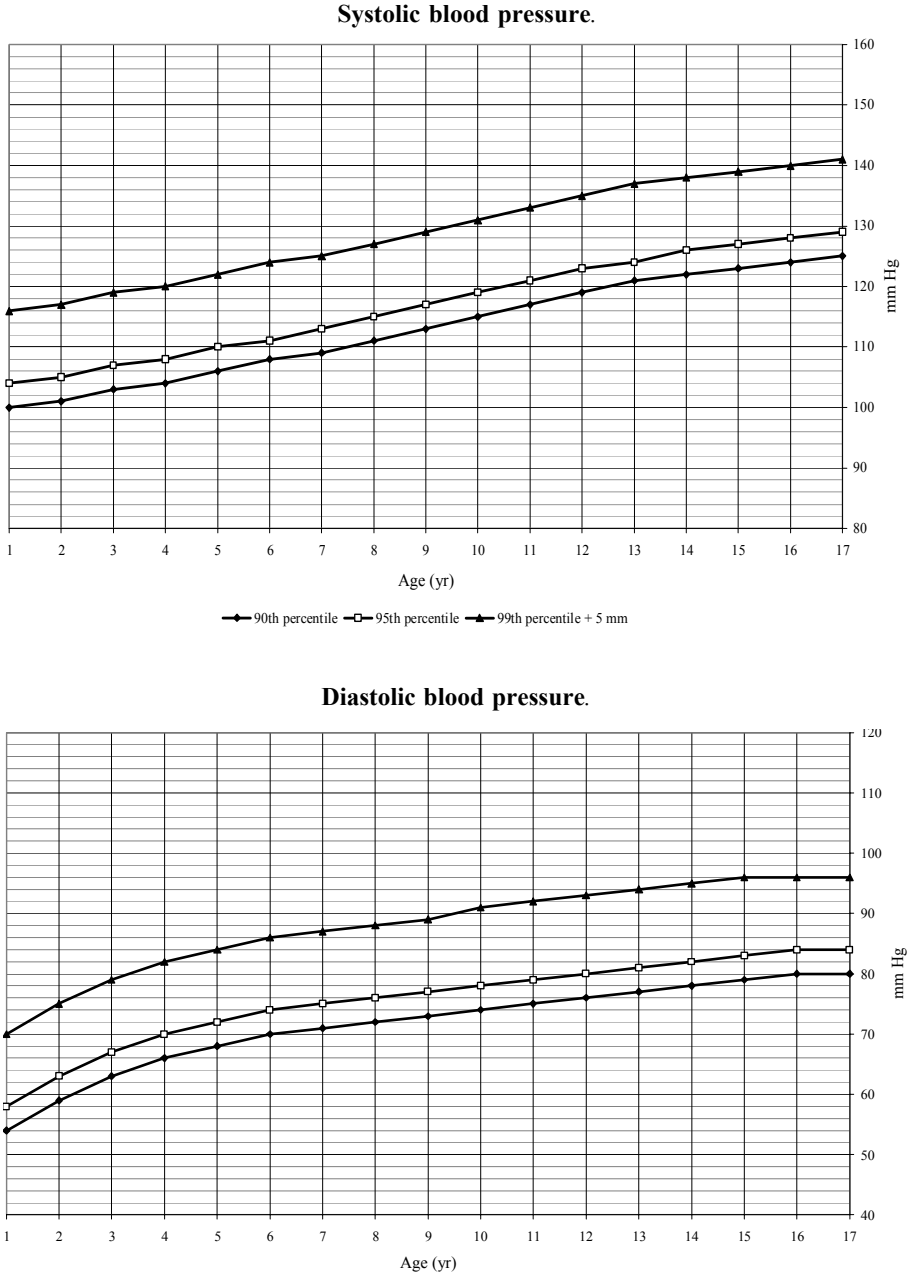

Fig. 2. *Blood pressure levels for girls at 50th percentile for height. Chart depicting 90th (closed diamonds), 95th (open circles) and 99th + 5 mm (closed triangles) percentile values for (a) systolic and (b) diastolic blood pressures, representing cut off values for the diagnosis of pre-hypertension, stage I and stage II hypertension respectively in girls (based on reference 4).*

level and the observer's eye at the level of the mercury column. Choosing the correct cuff size is crucial since a small cuff might overestimate the readings and vice versa (*Table III*). The width of the cuff bladder should be 40% of the arm circumference midway between the olecranon and the acromion and its length 80-100% of the arm circumference. If an appropriate cuff size is not available, the next larger size is used(4).

With the stethoscope on the brachial artery, the mercury column is lowered slowly (2 mm per second). Systolic blood pressure is the point when

Korotkoff sounds are first heard (K1) and disappearance of sounds (K5) is the diastolic pressure. If Korotkoff sounds persist, the measurement is repeated with less pressure on the stethoscope head. If the sounds persist at low intensity, then K4 (muffling of sounds) is recorded as the diastolic pressure. Blood pressure recordings should be expressed to the nearest 2 mm Hg. A high reading should be confirmed after the child has rested for 5 minutes and the average of 2-3 readings is taken as the value for that occasion.

Transient hypertension

Hypertension may be transient in certain conditions, *e.g.*, acute glomerulonephritis, acute intermittent porphyria, Guillain Barre syndrome, raised intracranial pressure, corticosteroid administration, anxiety and hyperthyroidism. Therapy for hypertension may be required in some cases. Persistence of elevated blood pressures requires detailed evaluation.

TABLE III–*Dimensions for Blood Pressure Cuffs*

Age	Width (cm)	Length (cm)
Newborn, infant	4	8
Child	9	18
Adolescent	10	24
Adult	13	30
Thigh	20	42

TABLE IV–*Causes of Persistent Hypertension*

Renal parenchymal disease: Chronic glomerulonephritis, reflux nephropathy, obstructive uropathy, polycystic kidney disease, renal dysplasia
Renovascular hypertension: Idiopathic aortoarteritis (Takayasu disease), renal artery stenosis, renal artery thrombosis
Cardiovascular disease: Coarctation of aorta
Primary (essential) *hypertension*
**Endocrine:* Pheochromocytoma, Cushing syndrome, congenital adrenal hyperplasia, primary hyperaldosteronism, Liddle's syndrome, syndrome of apparent mineralocorticoid excess, glucocorticoid remediable aldosteronism, neuroblastoma
**Renal tumors:* Wilms' tumor, nephroblastoma

* Rare

Sustained hypertension

Sustained hypertension in children is often secondary to an underlying renal disease (*Table IV*); approximately 60-70% patients have renal parenchymal disorders and 5-25% has renovascular disease(11,12). Coarctation of aorta is an important cause during infancy. In recent years, essential hypertension has become an important health concern. Patients with essential hypertension are usually postpubertal and over-weight; they typically show stage 1 hypertension and have no evidence of target organ damage.

Clinical features and complications

Most patients with pre-hypertension and hypertension are asymptomatic or have non-specific symptoms(13). Infants may show irritability, failure to thrive, vomiting, feeding problems, seizures or respiratory distress(4). The occurrence of epistaxis is rare.

Acute complications (hypertensive crises)

Patients with stage 2 hypertension are at risk for hypertensive crises, which are classified as emergencies or urgencies, based on the respective presence or absence of acute end organ damage (*e.g.*, hypertensive encephalopathy, intracerebral bleeding, acute left ventricular failure and renal failure). The occurrence of these complications is related to the rate of rise and duration of hypertension, rather than absolute blood pressure values(14,15).

Hypertensive encephalopathy is characterized by lethargy, dullness, headache, seizures and visual disturbances including blindness. Cerebral infarction, hemorrhage and facial nerve palsy may occur(11). Neuroimaging shows features of white matter degeneration in the parieto-occipital area (posterior leukoencephalopathy), which are reversible with treatment(14). Examination of the retina might shows hemorrhages, exudates or papilledema. Acute left ventricular failure is another life-threatening complication of severe hypertension.

While hypertensive emergencies require reduction of blood pressure within hours, the same

can be achieved over 2-3 days in patients with hypertensive urgencies.

Chronic complications (target organ damage)

Sustained hypertension results in changes in eyes (hypertensive retinopathy), heart (increased left ventricular mass, diastolic dysfunction), kidneys (albuminuria), brain and blood vessels (increased initimal and medial thickness). There is evidence that these changes are common, even in patients with long standing stage 1 hypertension(4,16).

Evaluation

Careful history and physical examination provide clues to the underlying etiology (*Table V*). History is taken for dietary habits, abdominal trauma, physical activity, and symptoms related to renal, cardiac or thyroid disorders. Infants are assessed for history of oligohydraminos and invasive procedures in NICU (*e.g.*, umbilical artery catheterization). Family history is taken for hypertension, diabetes, dyslipidemia, obesity, premature cardiovascular or cerebrovascular disease and renal disorders.

The patient's height and weight are measured and body mass index (BMI) calculated. Patients who are overweight or obese are at risk for essential hypertension. The peripheral pulses should be palpated, and blood pressure measured in both arms and at least one lower limb; pressure in the lower limbs normally exceeds that in the upper extremities by 10-20 mm Hg(4).

Investigations

Secondary hypertension must be considered in every child or adolescent who presents with elevated blood pressures. Since the majority of patients with secondary hypertension has a renal or renovascular etiology, screening tests are designed to evaluate for these conditions (*Table VI*). All patients with hypertension should also be screened for target organ damage.

The extent of evaluation depends on the patient's age, severity and duration of hypertension, presence of target organ damage and family history. Prepubertal patients, and those with stage 2 hypertension, features of end organ damage or underlying disorders are evaluated in detail. An obese adolescent with stage 1 systolic

TABLE V–*Clinical Features Indicating Underlying Diagnosis*

Underlying cause	Feature
Renal parenchymal, urological	Facial puffiness, edema, abdominal pain, dysuria, hematuria, frequency, polyuria; history of urinary tract infections; abdominal mass
Renovascular, coarctation of aorta	Asymmetric pulses, abdominal/neck bruit, weak femoral artery pulses, café au lait spots, neurofibromatosis
Connective tissue disease	Arthritis, arthralgias, unexplained fever, polymorphic rash
Endocrine	Muscle weakness, cramps; episodic fever, pallor, sweating, flushing, tachycardia; polyuria, polydipsia, failure to thrive; abdominal mass; ambiguous genitalia/ virilization

TABLE VI–*Basic Diagnostic Work Up*

Evaluation for cause
Hemogram
Blood urea, creatinine, electrolytes
Fasting lipids, glucose, uric acid
Urinalysis, culture
24-hr urinary protein or spot protein to creatinine ratio
Chest *X*-ray
Renal ultrasonography
Screen for target organ damage
Retinal fundus examination
Urine: microalbumin, spot protein to creatinine ratio
Chest *X*-ray, ECG, echocardiography

hypertension, baseline tachycardia, family history of hypertension, and normal history and physical examination needs no more than the basic evaluation (*Table VI*).

Based on clinical features and initial evaluation, a cause for hypertension is suggested in most instances. Confirmation of the diagnosis requires specific investigations tailored to specific needs (*Table VII*). Occasionally, the cause for hypertension may not be found despite detailed evaluation. Judicious use of radionuclide and biochemical investigations, conducted in collaboration with a pediatric nephrologist, is recommended in such cases.

Management

It is useful to distinguish essential from secondary hypertension. While the initial management for patients with essential hypertension comprises of life style modifications (see below), most patients with sustained secondary hypertension require treatment with antihypertensive agents(4).

Pre-hypertension

Patients are primarily managed by lifestyle modifications (see below) and revaluated 6 months later. The parents of these children are informed and advised regarding careful follow up. Medications are not required unless the patient has comorbid conditions (*e.g.*, chronic kidney disease, diabetes mellitus or dyslipidemia) or evidence of target organ damage.

Essential hypertension

Patients with essential hypertension are initially managed with lifestyle modifications. Pharmacological therapy is initiated if there is (i) a comorbid condition (chronic kidney disease, diabetes mellitus or dyslipidemia), (*ii*) target organ damage or (*iii*) failure of blood pressure to decline below the 95th percentile, despite lifestyle modifications, for 6 months.

Lifestyle modifications

Lifestyle changes are recommended for all children with hypertension; interventions based on daily routines are likely to be more successful.

Weight reduction

Achievement of ideal body weight is important, since reduction of weight reduces sensitivity of blood pressure to salt and attenuates cardiovascular risk factors, *e.g.*, dyslipidemia and insulin resistance. Reduction of BMI by 10% is reported to lead to 8-12 mm Hg fall in systemic blood pressure(4). Weight reduction should be achieved by regular physical activity and diet modification. Prevention of excess weight gain limits future increases in blood pressure.

TABLE VII–*Additional Diagnostic Tests for Sustained Hypertension*

Condition	Diagnostic investigations
Glomerulonephritis	Complement (C3), ANA, ANCA, anti-dsDNA, renal biopsy
Reflux nephropathy	Micturating cystourethrogram, DMSA scintigraphy
Renovascular hypertension	Doppler flow studies, captopril renography Angiography (MR, spiral CT, digital subtraction or conventional) Renal vein renin activity
Coarctation of aorta	Echocardiography, angiography
Endocrine causes	Thyroxine, thyroid stimulating hormone Plasma renin activity, aldosterone Plasma and urinary cortisol Plasma and urine catecholamines; MIBG scan, CT/MR imaging

ANA antinuclear antibody, ANCA antineutrophil cytoplasmic antibody, anti-dsDNA, anti-double stranded DNA antibody, DMSA demercaptosuccinic acid, MIBG meta-iodobenzyl guanidine.

Increased physical activity

Children are encouraged to be active not only for weight control but for their well being. While they often find defined physical exercises (aerobics, tread mills) boring, they are likely to continue activities incorporated into their routines, *e.g*., walking or cycling to school, playing with friends outdoors and swimming. The Group supports the recommendations of 30-60 minutes or more of physical activity every day that is developmentally appropriate, enjoyable and involving a variety of activities(17). Adolescent girls in our country should be specifically targeted, since they spend considerably less time than boys in outdoor sport.

Participation in competitive sports is avoided in patients with stage 2 hypertension or target organ damage, until blood pressure is controlled satisfactorily. Strength training (isometric) exercises (*e.g*., weight lifting, gymnastics, karate and judo) should be avoided.

Dietary changes

Direct evidence on the benefits of dietary changes from rigorous, well-controlled trials in children and adolescents is sparse. Accordingly, the effect of diet on blood pressure in children is extrapolated chiefly from studies on adults.

Recommendations for daily sodium intake in children range between 1-1.5 g (45-65 mEq sodium, 2.6-3.8 g salt). Dietary sodium restriction is associated with small reductions in blood pressure in children(4,19). A 'no added salt diet' is a satisfactory approach to restrict salt intake. Intake of food products high in sodium (processed and canned foods, items prepared in fast food shops including pizzas, pickles and salted potato chips) should be avoided. Increased potassium intake, through vegetables and fruits, is associated with modest reduction of systolic and diastolic blood pressure in adults with essential hypertension(19). Potassium intake should however be restricted in children with chronic kidney disease with glomerular filtration rate (GFR) below 30 mL/min/1.73 m^2, adrenal insufficiency, severe heart failure, or those receiving treatment with angiotensin converting enzyme inhibitors (ACEI), non-steroidal anti-inflammmatory agents and potassium sparing diuretics. Despite suggestions that foods rich in calcium, magnesium, folic acid and fiber are useful in reducing blood pressure, there is limited evidence in this regard.

An increased intake of fresh vegetables and fruits, whole grains and non-fat dairy is recommended. These foods are low in sodium and saturated fat and rich in minerals (potassium, calcium, magnesium) and fiber. The Group endorses the dietary recommendations of the IAP Consensus Committee on Obesity(20). The daily food composition is considered a 'thali', where half (50%) is vegetables, salads and fruits, a quarter (25%) is cereals (rice and/or chapattis), and the remainder is protein based (legumes, milk, egg, animal protein). The intake of fried foods, snacks and sweet dishes should be limited.

Secondary hypertension

Patients with sustained secondary hypertension require therapy with antihypertensive agents. Physicians should be aware of the risk of hypertensive emergencies in children with stage 2 hypertension. The need to adhere to healthy eating habits and lifestyle is emphasized.

Drug therapy

Drug therapy is indicated in patients with (*i*) acute or chronic complications of hypertension, including evidence of target organ damage, (*ii*) secondary hypertension, (*iii*) stage 2 hypertension, (*iv*) stage 1 hypertension that persists despite 6-months' of lifestyle modifications, and (*v*) pre-hypertension or stage 1 hypertension with comorbid conditions (diabetes, chronic kidney disease or dyslipidemia).

Principles of treatment

- The goal for treatment is reduction of blood pressure to levels <95th percentile, unless comorbid conditions or target-organ damage is present, when it should be lowered to <90th percentile.
- Commonly used medications in children include ACEI, calcium channel blockers (CCB), vasodilators, β blockers and thiazide

TABLE VIII–*Oral Antihypertensive Medications*

Agents	Dose; frequency	Comments
Angiotensin converting enzyme inhibitors, angiotensin receptor blockers		
Captopril	0.3 - 6 mg/kg/day; tid	Use cautiously if GFR <30 ml/min/1.73 m^2; avoid in renal artery stenosis
Enalapril	0.1 - 0.6 mg/kg/day; qd	Use smaller doses in neonates
Lisinopril	0.06 - 0.6 mg/kg/day; qd	Monitor serum potassium, creatinine regularly
Ramipril	6 mg/m^2; qd	Side effects: hyperkalemia, impaired renal functions; anemia, neutropenia, dry cough infrequent
Irbesartan	4-5 mg/kg/day	
Losartan	0.7 - 1.4 mg/kg/day; qd	
Calcium channel blockers		
Amlodepine	0.05 - 0.5 mg/kg/day; qd-bid	Extended release nifedepine must be swallowed whole
Nifedipine (extended release)	0.25 - 3 mg/kg/day; qd-bid	Side effects: Headache, flushing, dizziness, tachycardia; at higher doses: lower extremity edema, erythema
Isradipine	0.15 - 0.8 mg/kg/day; tid	
Beta-blockers		
Atenolol	0.5 - 2 mg/kg/day; qd-bid	Atenolol: decrease dose by 50% at GFR <50 ml/min/1.73 m^2; give on alternate days at GFR <10 ml/min/1.73 m^2
Metoprolol	1 - 6 mg/kg/day; bid	Sleep disturbances with propranolol, metoprolol; hyperlipidemia
Propanolol	1 - 4 mg/kg/day; tid	Avoid in asthma, heart failure; blunt symptoms of hypoglycemia
Labetalol	1 - 40 mg/kg/day; bid-tid	
Central alpha agonist		
Clonidine	5 - 25 µg/kg/day; tid-qid	Abrupt cessation may cause rebound hypertension; sedation
Peripheral alpha antagonist		
Prazosin	0.05 - 0.5 mg/kg/day; bid-tid	May cause 'first dose' hypotension, syncope
Vasodilators		
Hydralazine	1 - 8 mg/kg/day; qid	For hypertension refractory to other drugs
Minoxidil	0.1 - 1 mg/kg/day; qd-bid	Side effects: headache, palpitation, fluid retention, congestive heart failure; pericardial effusions, hypertrichosis with minoxidil
Diuretics		
Frusemide	0.5 - 6 mg/kg/day; qd-bid	Monitor electrolytes, fluid status periodically
Spironolactone*	1 - 3 mg/kg/day; qd-bid	Thiazides: dyslipidemia, hyperglycemia, hyperuricemia, hypokalemia, hypomagnesemia
Metolazone	0.2 - 0.4 mg/kg/day; qd	Loop diuretics: metabolic alkalosis, hypokalemia, hypercalciuria
Hydrochlorothiazide	1 - 3 mg/kg/day; qd	*Use cautiously with ACEI, angiotensin receptor blockers
Amiloride*	0.4 - 0.6 mg/kg/day; qd	

qd once daily; bid twice daily; tid thrice daily; qid four times daily

diuretics (*Table VIII*).

- Therapy is initiated with one agent, at an appropriate dose and the dose is increased until the desired blood pressure is achieved. If the highest dose is not effective or if there are side effects, a drug from a different class is added or substituted.
- Medications with a longer duration of action (once, twice daily dosing) are preferred for better compliance and less side effects.
- Dose adjustment of antihypertensive medications need not be made more frequently than every 2-3 days.

An approach to the treatment of hypertension is

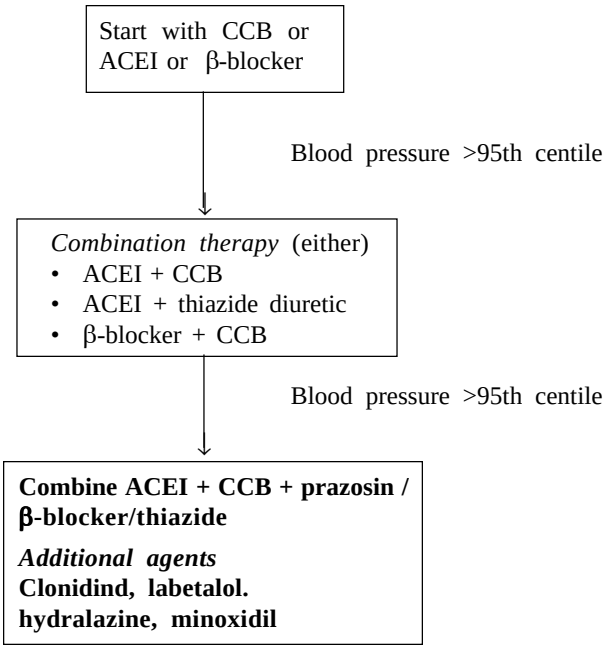

Fig. 3. Therapy is initiated with a calcium channel blocker (CCB), angiotensin converting enzyme inhibitor (ACEI) or β adrenergic blocker. If two drugs are required, the ACEI (or β-blocker) should be combined with a CCB. Unsatisfactory control of blood pressure requires the use of additional agents.

shown in *Fig. 3*.

Nifedipine and amlodipine are effective CCB for children. The availability of long acting preparations permits once or twice daily dosing. Sustained release preparations of nifedipine should be swallowed whole, and not crushed or chewed. Captopril, chiefly used in young infants, requires dosing every 6-8 hr. Beyond infancy, enalapril (1-2 daily doses) is preferred. Newer ACEI (lisinopril, ramipril) require once daily dosing and have fewer side effects. Angiotensin receptor blockers used in children include losartan, valsartan and irbesartan. Cardioselective β-blockers (atenolol, metoprolol) are effective agents, requiring once or twice daily dosing and have few side effects. The use of propranolol is limited in view of the need for multiple daily doses and side effects. Labetalol, a α- and β-blocker, is useful in patients refractory to other medications.

Combinations minimize the side effects by allowing administration of lower dosage of different agents. With combination therapy, consideration must be given to combining drugs with complementary mechanism of action, *e.g.*, ACEI (or angiotensin receptor blocker) with a CCB or thiazide diuretic, or vasodilator with diuretic or β blocker (*Fig. 3*). While combinations of ACEI and angiotensin receptor blocker have been proposed for adults, similar experience is limited in children(21). Long term combination of thiazides with β-blockers may be associated with an increased incidence of glucose intolerance(22).

Specific recommendations

The choice of medication also depends on the cause of hypertension and associated complications.

Essential hypertension: While there is no consensus on the appropriate initial therapy, the choices are between CCB and ACEI. Therapy with β-blockers is recommended in patients who cannot tolerate ACEI or CCB(22).

Acute glomerulonephritis: Hypertension in post-infectious glomerulonephritis is of short duration and associated with salt and water retention. Fluid and sodium restriction and judicious use of loop diuretics are useful in patients with circulatory congestion, hypertension and edema. Severe hypertension with or without encephalopathy is an emergency and usually responds to treatment with CCB and furosemide. Occasionally treatment with a β-blocker or ACEI may be necessary.

Chronic kidney disease: The target blood pressure in these patients is <90th percentile. For patients with chronic kidney disease stage I-III (GFR >30 mL/min/1.73 m^2) therapy should be initiated with ACEI, since these agents also reduce proteinuria and retard progression of renal damage(23). Monitoring of serum potassium and creatinine is necessary, initially at 7-14 days and then every 1-3 months. The dose of ACEI (or angiotensin receptor blockers) is reduced if serum creatinine exceeds 30-35% from the baseline or there is hyperkalemia. Treatment with ACEI should be avoided in patients with advanced chronic kidney disease (stage IV-V; GFR <30 mL/min/1.73 m^2). Therapy in these cases is initiated with either a CCB or β-blocker.

Guidelines for managing hypertension in

patients with chronic kidney disease also include:

- Sodium intake is restricted to between 1-1.5 g (45-65 mEq sodium, 2.6-3.8 g salt).
- Co-administration of diuretics helps in reducing sodium and volume overload. Thiazides (hydrochlorothiazide, chlorthalidone) are satisfactory, but not effective at GFR <30 mL/min/1.73 m^2.
- Additional medications include α-blockers (prazosin, labetalol), centrally acting agents (clonidine) or vasodilators (hydralazine, minoxidil).
- The dosage of some medications (*e.g.*, atenolol) need modification in renal impairment (*Table VIII*).

Renovascular disease: In patients with high probability or confirmed renovascular disease, therapy should be initiated with a CCB or/and a β-blocker. Additional agents include prazosin, labetalol, clonidine, hydralazine and/or minoxidil. While therapy with ACEI or angiotensin receptor blockers is avoided in patients with suspected or confirmed bilateral renovascular disease, these agents might be used cautiously in those with unilateral renovascular hypertension.

Complications of hypertension

ACEI are the preferred initial agents in subjects with ventricular dysfunction. Additional therapy may be given with loop or thiazide diuretics, β blockers and aldosterone antagonists. ACEI or angiotensin receptor blockers are recommended for patients with associated proteinuria.

Drug step-down

Overweight children with uncomplicated essential hypertension, who successfully lose weight, are best candidates for "step-down" treatment. This approach attempts a gradual reduction of the medication after 8-12 months of satisfactory blood pressure control. Patients must maintain a healthy lifestyle and blood pressure should be checked regularly (q 3 months) after cessation of therapy. Step down of drug therapy might also be possible in patients in whom a specific intervention has ameliorated the underlying cause for hypertension, *e.g.*, following resection of pheochromocytoma or balloon dilatation for renovascular disease.

Monitoring

Patients and their families should receive counseling for cardiovascular risk factors and dyslipidemia, and continued emphasis on lifestyle modifications. Blood pressure is monitored every 3 months. Screening for end organ damage and renal dysfunction (proteinuria, serum creatinine) and surveillance for side effects of drugs is required annually.

Hypertensive emergencies

Patients with stage 2 hypertension may present with acute, life threatening target organ damage involving central nervous system (encephalopathy, seizures), heart (pulmonary edema) or kidneys (acute renal failure). These patients need hospitalization for monitoring and supportive care. Blood pressure levels are usually 5-15 mm above the 99th percentile, and should be reduced to safe levels. Rapid reduction of blood pressure might, however, compromise blood flow and result in ischemic complications in the brain, retina, spinal cord and kidneys. Blood pressure reduction, therefore, must be regulated in order to prevent end organ damage to these organs(24).

The difference between the observed and desired (95th percentile) blood pressure is estimated; 25-30% of the desired reduction should occur in the first 3-4 hr, another 25-30% in the next 24 hr, and then to the desired level over next 2 days. Agents of choice include short acting, intravenous (IV) preparations that are titrated to response (sodium nitroprusside, nitroglycerine, labetalol and nicardipine) (*Table IX*). Therapy with enteral antihypertensive drugs should be instituted within 6-12 hr of parenteral therapy, and the latter gradually withdrawn over the next 12-24 hr.

Sodium nitroprusside is the agent with the longest track record, readily available and the least expensive of all parenteral drugs. This agent can be used in most hospital settings, provided there is

TABLE IX – *Management of Hypertensive Emergencies*

Drugs	Dose	Comments
Sodium nitroprusside	IV infusion: 0.3-8 μg/kg/min (in 5% dextrose) Protect infusate from light	Onset of action at 30 seconds; peaks 2 min; disappears within 3 min of stoppage Medication for >48 hr at dose of >3 μg/kg/minute might cause cyanide toxicity (dizziness, confusion, seizures, jaw stiffness and lactic acidosis), which is treated with amyl nitrate, sodium nitrate and hemodialysis IV infusion of sodium thiosulfate (one-tenth dose of nitroprusside) or hydroxycobalamin prevents toxicity
Nitroglycerine	IV infusion: 1-3 μg/kg/min, increase 1 μg/kg/min q 30 min	Onset of action at 2-5 min; duration 5-10 min after discontinuation Alternative to nitroprusside (especially in adults with coronary artery disease) Methemoglobinemia, headache, tachycardia may occur; tachyphylaxis on prolonged use
Labetalol	IV infusion: 0.25-3 mg/kg/hr; or bolus: 0.2-1 mg/kg/dose; may repeat q 5-10 min to maximum 40 mg	Onset of action within 5-10 min; duration 3-6 hr Orthostatic hypotension, abdominal pain, diarrhea may occur Avoid in patients with asthma, heart failure or heart block
Nifedipine	PO: 0.25 mg/kg	Unpredictable and often uncontrolled fall of blood pressure; might be used if no access to parenteral agents
Nicardipine	IV infusion: 0.5-5 μg/kg/min; maximum 5 mg/hr	May cause reflex tachycardia, increase cyclosporine levels Avoid in head trauma, intracranial hemorrhage
Phentolamine	IV bolus: 0.1-0.2 mg/kg (maximum 5 mg); repeat 2-4 hr	Used for pheochromocytoma; administer 1-2 hr prior to surgery May cause reflex tachycardia

facility for monitoring of blood pressure. Initially infused at a rate of 0.3-0.8 mg/kg per minute, the dose may be increased in increments of 0.1-0.2 mg/kg per minute, every 15 minutes, if the desired reduction is not achieved. Blood pressure is measured at least every 15 minutes; pupillary reflexes, visual acuity and level of consciousness are also monitored. Two IV lines should be maintained, one for drug infusion and the other for saline infusion (if the blood pressure were to fall precipitously). Loss of pupillary reflex to light is an early indicator of retinal vascular ischemia, requiring immediate infusion of normal saline. Patients receiving nitroprusside at doses exceeding 2-3 mg/kg per minute for longer than 48 hr are at risk of cyanide toxicity, and even earlier if there is hepatic or renal dysfunction.

Experts have discouraged the use of immediate release sublingual or oral nifedipine for hypertensive emergencies in adults, since sudden reduction of blood pressure might lead to arrhythmias, syncope, cerebrovascular accidents and myocardial infarction. These complications are rarely reported in children, and nifedipine has been used safely and effectively, by pediatricians, for hypertensive emergencies(25). The risks of side effects due to sudden fall of blood pressure are limited, particularly if the dose of nifedipine is between 0.1-0.25 mg/kg(26). Physicians should however be aware that the response to short acting nifedipine might be inconsistent and unpredictable (requiring more than one dose) or uncontrolled (sudden fall of blood pressure).

Volume depletion is common in patients with severe hypertension and IV administration of loop diuretic together with a potent anti-hypertensive agent might lead to a precipitous drop in blood pressure. Diuretics should therefore be avoided unless specifically indicated for volume overload as occurs in glomerulonephritis coexisting pulmonary edema.

Hypertensive urgencies

Hypertensive urgencies differ from emergencies in having no evidence of acute target organ damage. Patients have stage 2 hypertension and less dramatic symptoms (*e.g.*, headache and/or vomiting), but are at risk for progression to hypertensive emergencies. Controlled reduction of blood pressure, using oral medications, over several hours is desirable. Effective oral agents include nifedipine, clonidine and labetalol.

The onset of action of nifedipine (0.25 mg/kg, maximum 10 mg) administered orally is within 5-10 min, peaks at 30-60 min and lasts for 2-6 hr. While children show reflex tachycardia, the occurrence of serious complications with the use of oral nifedipine in this situation is rare. Oral administration of clonidine (0.05-0.1 mg) is also effective, although the onset of action (30-60 min) and peak effect (2-4 hr) is delayed. Sedation and orthostatic hypotension occurs in many patients. Sublingual or oral administration of captopril (6.25-25 mg) also shows a rapid onset (10-30 min) and peak (1-2 hr), and relatively prolonged duration of action (4-8 hr). Despite overall efficacy of the above agents, a predictable reduction of blood pressure is often not possible. Patients with hypertensive urgencies should be observed closely, since use of IV medications might be required.

Neonatal hypertension

The management of hypertension in neonates was not separately addressed by the Expert Group. Blood pressure in neonates is determined by birth weight and gestational age. Renovascular (renal artery or venous thrombosis) and renal parenchymal disorders are important causes of hypertension. Newborns with severe hypertension are managed with continuous IV infusion of nitroprusside or labetalol. Effective oral agents include CCB, hydralazine and minoxidil; ACEI should be administered at lower doses.

Conclusions

The above guidelines represent a consensus view based on evidence and opinion of experts of the Indian Pediatric Nephrology Group. Measurement of blood pressure is an important component of pediatric physical examination that enables screening for hypertension. Elevated blood pressure in children may be a sign of an underlying disease or represent early onset

essential hypertension. Pediatricians should be aware of the principles of early detection, evaluation and management of such patients. Children with hypertension need long term follow up, counseling and treatment, which should be achieved by their primary pediatricians in collaboration with pediatric nephrologists.

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